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Theory of mind in bipolar disorder and its comparison to the impairments observed in schizophrenia.

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Theory of mind in bipolar disorder, with comparison to the impairments observed in schizophrenia.

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Abstract

Our ability to make sense of information on the potential intentions and dispositions of others is of paramount importance for understanding their communicative intent, and for judging what an appropriate reaction might be. Thus anything that impinges on this ability has the potential to cause significant social impairment, and compromise an individual's level of functioning. Both bipolar disorder and schizophrenia are known to feature theory of mind impairment. We conducted a theoretical review to determine the extent and types of theory of mind impairment in bipolar disorder, and evaluate their relationship to medication and symptoms. We also considered possible mediatory mechanisms, and set out to discover what else could be learnt about the impairment in bipolar disorder by comparison to the profile of impairment in schizophrenia. The literature established that in bipolar disorder (i) some form of theory of mind impairment has been observed in all mood states, including euthymia, (ii) the form of theory of mind assessed and task used to make the assessment influence the impairment observed, and (iii) there might be some relationship to cognitive impairment, although a relationship to standard clinical variables was harder to establish. What also became clear in the literature on bipolar disorder itself was the possible relationship of theory of mind impairment to history of psychotic symptoms. Direct comparative studies including patients with schizophrenia were thus examined, and provided several important directions for future research on the bases of impairment in bipolar disorder. Particularly prominent was the issue of whether theory of mind impairment could be considered a candidate endophenotype for the psychoses, although current evidence suggests this may be premature. The differences in impairment across schizophrenia and bipolar disorder may, however, have genuine differential effects on social functioning and the likely success of remediation.

Keywords: bipolar disorder, psychoses, schizophrenia, social cognition, theory of mind.

Word Count: 9,890

'Social cognition' describes the mental operations that underlie social interactions, including perceiving, interpreting and generating responses to the intentions, dispositions and behaviours of others (Green et al., 2008). 'Theory of mind' is a crucial facet of social cognition, and can be defined as the ability to infer and predict the intentions, thoughts, desires, intuitions, behavioural reactions, plans and beliefs of other people (Green et al., 2008; Frith and Frith, 2011; Mathersul et al., 2013), through an awareness that others have a mind with mental states, information and motivations that may differ from one's own (Sabbagh, 2004; Korkmaz, 2011). Here cognitive theory of mind refers to the ability to make inferences about other people's beliefs, whereas affective theory of mind refers to the ability to make inferences about other people's feelings. A prominent feature of bipolar disorder is its significant negative impact on work-related, interpersonal and leisure activities (Elgie and Morselli, 2007). As theory of mind is so central to human life, any impairment of this cognitive capacity can only be detrimental to social functioning (Brune and Brune-Cohrs, 2006). The initial aim of this review is to further characterise the socio-cognitive profiles of patients with bipolar disorder by conducting a critical review of theory of mind in this patient group. This aim will be achieved via the presentation and synthesis of currently available published evidence. In recent years a number of reviews have either had to present broad overviews of theory of mind and other related social skills (Samame et al., 2012; McKinnon et al., 2013; Samame, 2013; Van Rheenen and Rossell, 2014; Samame et al., 2015), or evaluate evidence from a range of related diagnostic groups (Bora et al., 2009b; Hoernagl and Hofer, 2014). However, the recent surge of publications focussed on theory of mind in bipolar disorder allows us to now present a more focussed synopsis. In order to collate this evidence, a systematic search of the literature was conducted using the PsychINFO and Medline databases, covering the period from 1975 up to September 2015. The search terms used in examining these databases were (bipolar AND (disorder OR depression)) OR (mania OR manic) OR (euthymia OR euthymic) OR ((mood OR affective) AND disorder)) AND (("theory of mind") OR mindedness OR mentalising OR mentalizing). Review articles touching on social cognition in bipolar disorder were also examined to check for studies not captured by the search above, through backward citation searching. After reviewing the literature gathered by these means, the following areas of discussion were identified.

In the first part of the paper, we tackle the question of whether impaired theory of mind is characteristic across the mood states and whether it persists after symptomatic remission. Similarly we ask whether it is present in both bipolar I disorder and bipolar II disorder and consider whether it can be detected in related 'high-risk' or 'sub-syndromal' populations. We also examine the evidence for such impairments in paediatric samples. We then assess methodological factors which may have confounded previous research, such as the type of assessment used and demographic influences. Here we also highlight the seemingly varying scale of the problem and its breadth across different types of theory of mind. In the final section of part one, we seek to establish what the antecedents of impaired theory of mind are in bipolar disorder and what the symptom correlates of these deficits are. Medication effects are also considered. In achieving our initial aim, the hope is to generate information for clinicians who work with this patient group to help improve clinical outcomes (Mercer and Becerra, 2013).

In the second part of the paper, the aim is to review evidence on whether impaired theory of mind can be considered a trait-marker for psychosis across both affective and non-affective psychoses. Specifically, we ask whether patients with bipolar disorder and those with schizophrenia present with similar impairments. Here we do not set out to serve as a review of schizophrenic theory of mind per se, nor to make narrative comparisons between the separate literatures on theory of mind in the two disorders. Rather the purpose of this part of this paper is to establish the significance of data studies that have directly and quantitatively compared theory of mind abilities in the two disorders. Given the poorly understood origin of theory of mind deficits in bipolar

disorder, we evaluate the possibility that a link to psychosis should be an important line of enquiry (Bora et al., 2009b). Looking beyond the question of origin, could impaired theory of mind serve as a useful endophenotype of proneness to psychosis? We first tackle this question by reviewing studies of bipolar disorder which have compared the profile of impairment of theory of mind in bipolar patients who do and do not present with psychosis. We then move on to assessing studies which have explicitly contrasted theory of mind in schizophrenia vs. those in bipolar disorder. It is clear that theory of mind impairments in schizophrenia appear more severe than those in bipolar disorder. Reasons for the possible difference in size of impairment is examined, including both symptom and neurocognitive mediators. Close examination of the similarities and differences in theory of mind is important because of the impact of these deficits on social functioning, which in turn, might help explain the differences in outcome between schizophrenia and bipolar disorder (Donohoe et al., 2012).

We conclude the review by suggesting implications for clinical management and propose next steps for research on theory of mind in bipolar disorder and its possible role as a trait marker for psychosis.

1. Impairments of theory of mind in bipolar disorder

Given that impaired social cognition in patients with serious mental illness impacts on increased symptom severity, prolonged course of illness, higher rates of relapse and daily functioning, characterisation of the extent of these deficits is important (Henderson, 2013; Hoertnagl and Hofer, 2014; Weightman et al., 2014). Although bipolar disorder is commoner than schizophrenia, theory of mind in this condition has been under-explored relative to its study in schizophrenia (Brune and Brune-Cohrs, 2006). We summarise current literature for the reader in **Table 1**.

1.1 The clinical generalisability of impairments across sub-groups

One issue that has complicated the study of theory of mind in bipolar disorder is that this diagnostic label actually comprises a group of disorders with heterogeneous clinical presentation, course and outcome (Duffy, 2014; Hasler and Wolf, 2015). Not only does the clinical course change as a patient cycles through recurrent depressive, manic and sometimes mixed mood states (Phillips and Kupfer, 2013), there are subtypes of bipolar disorder based on the severity of mania experienced, variable occurrence of psychosis within these subtypes (Parker et al., 2013), and related sub-syndromal bipolar subtypes to contend with (Leboyer and Kupfer, 2010). There has as yet, been little systematic comparison of impairments in theory of mind across all subtypes, even though the variability in clinical presentation might seem to necessitate it (Schenkel et al., 2014). It is likely that inconsistent results in the past may have partly reflected the heterogeneous presentation of bipolar disorder (Samame, 2013), the mixed nature of samples, and even indiscriminate mixing of samples with other affective disorders such as major depression (Inoue et al., 2004; Martino et al., 2011). Whilst the socio-cognitive profile of bipolar disorder across mood states is somewhat unclear (Hoertnagl and Hofer, 2014), currently available evidence suggests that some form of impairment exists whatever the symptomatic phase of illness (Bora et al., 2015).

In one of the first studies to compare the performance of patients experiencing a depressed vs. manic mood state, the performance of both groups was impaired relative to healthy controls (Kerr et al., 2003). In a first-order 'false-belief' task, the ability to understand that someone can hold a belief

that is different from the actual state of affairs is assessed, whereas in a second-order false-belief task, participants have to infer the (false) beliefs of one character about the (false) beliefs of a second character (Frith and Corcoran, 1996). Kerr et al.'s data from such a False Belief Task showed that both groups were less able than healthy controls to correctly attribute mistaken beliefs about an object's location to predict or explain someone's behaviour. Similarly both patients in manic and depressed phases have demonstrated impairments (relative to healthy controls) on another classic theory of mind task known as the 'Picture Sequencing Task' (Langdon et al., 1997), in which participants sequence a series of cartoon picture stories that depict cooperation and deception, followed by explicit questions about characters' mental states (Wolf et al., 2010). These deficits persisted even when differences in age, intelligence and executive function were accounted for. Elsewhere, mixed manic/depressed patients have shown impaired performance on a series of theory of mind tasks relative to healthy controls (Ioannidi et al., 2015), including a false belief task, the 'Hinting task' which requires participants to infer from a subsequent hint what a character in a dialogue really meant (Corcoran et al., 1995), and the 'Faux Pas Recognition Test' (Baron-Cohen et al., 1999) in which participants have to recognise from a short text when a character commits a social error and says something it would be better not to say. However, no differences in performance were found in exploratory analyses of the effects of mixed/manic mood state vs. depressed and euthymic states in another study using the Picture Sequencing Task (Van Rheenen and Rossell, 2013b). Thus beyond there being evidence of theory of mind impairment across the different symptomatic phases which is suggestive of a potential trait marker, there is currently insufficient evidence to support the existence of a differential profile of impairment across the depressed, manic, hypomanic or mixed mood states.

A more tractable means of assessing whether theory of mind deficits in bipolar disorder represent a trait marker independent of mood state, has been to adopt the study of remitted or asymptomatic patients that are euthymic at the time of testing. Whilst one might expect subtler theory of mind impairments in euthymic patients, the effects observed are certainly not negligible. Two important meta-analytic pieces of work have estimated that the effects sizes for theory of mind impairment in the euthymic state are in the medium range ($0.5 < d < 0.8$) (Samame et al., 2012; Bora et al., 2015). Whilst the majority of studies of theory of mind in euthymic patients have found evidence of impairment (Bora et al., 2005; Olley et al., 2005; Montag et al., 2010; Barrera et al., 2013), this has not universally been the case. Kerr et al were not able to detect any difference in performance between their group of euthymic patients and healthy controls (Kerr et al., 2003). Purcell et al were also unable to detect impaired theory of mind when their euthymic patients performed the Reading the Mind in the Eyes Task, in which participants attempt to match photos of the eye region during facial expressions with the corresponding emotional mental state word, thereby constituting a form of affective theory of mind (Baron-Cohen et al., 2001; Purcell et al., 2013). Elsewhere, the deficits shown by euthymic patients performing the Reading the Mind in the Eyes affective theory of mind task became non-significant once neurocognitive impairments were controlled for (Martino et al., 2011). Studies of theory of mind in the euthymic state are, however, confounded by variable definitions of euthymia which have, for example, included a score <6 on the Young Mania Rating Scale (YMRS; (Young et al., 1978)) and a score <7 on the Hamilton Depression Rating Scale (HDRS; (Hamilton, 1960)) (Bora et al., 2005), a HDRS score <14 and a YMRS <5 (Montag et al., 2010), or a HDRS score <12 and YMRS <12 (Olley et al., 2005). These studies are thus potentially confounded by residual mood effects. Thus a distinction has thus been made between the performance of 'sub-syndromal' patients who score >7 but <15 on the HDRS, and truly euthymic patients who score <7 on the HDRS, with the performance of the former being more impaired than the latter (McKinnon et al., 2010). Nevertheless, beyond their theoretical importance, socio-cognitive deficits during euthymia are of notable clinical significance, given

168 evidence that such disturbances constitute an important obstacle for social reintegration and
169 rehabilitation (Barrera et al., 2013).

170 In the current Diagnostic and Statistical Manual of Mental Disorders classification system
171 (American Psychiatric Association, 2013), the severity of mania experienced by a patient with
172 bipolar disorder has specific diagnostic implications. Patients who have experienced a manic or
173 mixed episode that has lasted at least a week, or those who have experienced mania that is so severe
174 that it has required hospitalisation, are defined as having Bipolar 1 Disorder. In contrast, patients
175 who have experienced less-intense elevated (hypomanic) moods, but no full-blown manic or mixed
176 episodes, are defined as having Bipolar 2 Disorder. Most studies have so far focussed on the theory
177 of mind impairment in Bipolar 1 Disorder, however, some more recent studies have included
178 comparisons between Bipolar 1 and Bipolar 2 Disorder on the Picture Sequencing Task, the
179 Reading the Mind in the Eyes Task, and the Cognitive and Affective Perspective Taking Task in
180 which participants assess written scenarios and attribute characters' mental state or belief based on
181 cognitive or emotional information (Hynes et al., 2006). So far, none of these studies have found
182 any evidence to support a differential theory of mind impairment (Martino et al., 2011; Van Rheenen
183 and Rossell, 2013b; Schenkel et al., 2014).

184 Whilst differential theory of mind impairment have not yet been demonstrated based on
185 categorisation of bipolar disorder according to severity of mania, links have been found between
186 theory of mind impairment and the severity of certain aspects of hypomania e.g. mood lability.
187 Specifically, the study by Terrien et al. used the 'Yoni task' to assess the ability of healthy adults to
188 attribute cognitive and emotional mental states on the basis of verbal cues and gaze direction
189 (Terrien et al., 2014). In the Yoni task (Shamay-Tsoory et al., 2007), a trial comprises a cartoon
190 outline of the face of a character named Yoni, and four coloured pictures of objects belonging to a
191 single category (e.g. fruits, chairs) or faces, one in each corner of the computer screen. The
192 participant's task is to point to the correct answer (the image Yoni is referring to), based on a
193 sentence that appears at the top of the screen, and available cues such as Yoni's eye gaze and Yoni's
194 facial expression. With this task, Terrien et al. demonstrated that mood volatility showed a
195 relationship with theory of mind performance collapsed across cognitive and affective theory of
196 mind, but only in men. These findings raise the important issue of whether it is possible to detect
197 impaired theory of mind in populations at increased risk of developing bipolar disorder, either
198 through possession of traits and behaviours related to particular clinical dimensions, or through a
199 genetic predisposition to developing bipolar disorder. Does theory of mind impairment constitute a
200 useful cognitive endophenotype for bipolar disorder? In this vein, Reynolds et al. detected impaired
201 theory of mind in first-degree relatives of patients with bipolar disorder using the 'Strange Stories
202 Task' (Happé, 1994) in which participants read a series of stories and answer questions about
203 characters' mental states or physical events (Reynolds et al., 2014). However, in another relevant
204 study, children and adolescents with a parent with bipolar disorder who themselves exhibited some
205 mood dysregulation but did not meet the diagnostic criteria for bipolar disorder, appeared
206 unimpaired according to a task measuring recognition of mental states and identification of false
207 beliefs (Whitney et al., 2013). The predictive value of theory of mind impairments in 'at risk'
208 populations is therefore not yet clear (McKinnon et al., 2013), and further study of whether this
209 deficit antedates bipolar disorder or not is required. Work that searches to identify potential 'early
210 warning' signs is important, because identification of earlier stages of bipolar disorder prior to the
211 first manic episode, may help develop interventions to prevent or delay its onset (Ratheesh et al.,
212 2015).

214 In this section we have seen that there is a reasonable level of evidence to indicate that theory of
215 mind impairment is a feature of all mood states in bipolar disorder, although robust differential

patterns across the various subtypes are not yet supported. That is not necessarily to say that there are no such effects, at this early stage in the literature it may simply be that there has not yet been enough research. What are now needed are more systematic, well-controlled investigations. However, given the existence of any evidence of mood-state related impairments, heterogeneity needs to be taken into account in future research (Samame et al., 2015). Ideally, such investigation would be longitudinal and entail a patient acting as their own control whilst experiencing different mood states. Via such endeavours, a more well-grounded picture of the socio-cognitive profile of bipolar disorder across mood-states will emerge (Olley et al., 2005). The recent longitudinal study by Ioannidi et al. examining cognitive theory of mind impairment across both the remitted and symptomatic state is an excellent start in this respect (Ioannidi et al., 2015). Irrespective of theoretical implications, monitoring of theory of mind impairment in euthymic as well as symptomatic states has significant clinical value, since it might potentially prove a useful indicator of relapse potential in euthymia (Wolf et al., 2010;McKinnon et al., 2013;Mercer and Becerra, 2013;Terrien et al., 2014). Longitudinal analyses would also provide valuable information on the course of impact that theory of mind impairment has. Early work already suggests an association between affective theory of mind impairment and social functioning one year later (Purcell et al., 2013).

1.2 Methodological generalisability

Just as for the heterogeneity of mood states associated with bipolar disorder, the tasks used to assess theory of mind are heterogeneous in both content and form. To some extent, this has been a necessary evil, since theory of mind is not a unitary construct (Samame, 2013;Bora et al., 2015). Hence in this section, we consider both the pattern of differential impairment across different forms of theory of mind, and the possible influence of the theory of mind test used. It would perhaps be premature to assume that cognitive and affective theory of mind are equally affected by bipolar disorder, given the putative evidence for the (partial) separability in functional neuroanatomy (Mitchell and Phillips, 2015) of these two types, and their differing component sub-processes. Indeed, there is evidence for differential behavioural impairment in other populations, including old age, schizophrenia, autism and neurodegenerative disease (Poletti et al., 2012;Wang and Su, 2013;Chung et al., 2014). Using the Reading the Mind in the Eyes Task to index affective theory of mind and the Faux Pas test to index cognitive theory of mind, Barrera et al. directly compared the performance of euthymic patients on these two forms of theory of mind. Whereas the patients with bipolar disorder did show impairment relative to healthy controls on the cognitive theory of mind test, they were not impaired on the affective theory of mind test (Barrera et al., 2013). Here the authors argued that the lack of impairment for affective theory of mind might reflect the relative lack of mood disturbance in euthymic patients. This suggestion is in accord with findings in three more-controlled studies of a greater impairment of cognitive theory of mind in bipolar disorder than affective theory of mind using questions about feeling vs. thinking within the same task (Shamay-Tsoory et al., 2009;Montag et al., 2010;Schenkel et al., 2014). However, in the Schenkel et al. study, the patients were experiencing an acute episode of bipolar disorder, not euthymia (Schenkel et al., 2014). Hence the lack of current affective disturbance typically associated with euthymia cannot explain the lack of affective theory of mind impairment in that study. However, even though the cognitive and affective questions comprised part of the same task in the Schenkel et al. study, these questions still required different cognitive operations. Whereas the affective theory of mind questions required first-order mental state understanding and empathy (e.g. ‘how does the character feel’), the cognitive theory of mind questions entailed more advanced mental state reasoning and false belief understanding (e.g. ‘how a character might be misled into believing something is false based on false information from someone else’). Therefore at present, it cannot

be ruled out that differential impairment of cognitive vs. affective theory of mind might simply reflect a difference in degree of complexity or a difference in demand for linguistic processing. Overall, findings from a recent meta-analysis of performance of cognitive vs. affective theory of mind tasks by patients with bipolar disorder demonstrate that the differences noted above have not yet attained statistical significance across the body of current literature (Bora et al., 2015).

Differing processing demands are also relevant to the inconsistent impairments according to the tasks used to index the ability to make mental state inferences. For example, in one study, whilst patients with Bipolar 1 Disorder showed impairments on a first-order false belief task, the Hinting Task, and the Faux Pas Test, only impaired performance on the Faux Pas Test persisted when patients later transitioned into euthymia (Ioannidi et al., 2015). Similarly, in another study, first-degree relatives of patients with bipolar disorder demonstrated impairment on the Happé Strange Stories Test, but not the Reading the Mind in the Eyes Task, nor the Picture Sequencing Task (Reynolds et al., 2014). These differential task-dependent impairments have recently been quantified in a task-specific meta-analysis. In that work, small but significant effect sizes were obtained for differences in performance between patients and healthy controls with the Hinting and Reading the Mind in the Eyes Tasks (0.27 and 0.45 respectively), but a medium effect size was obtained for the difference in performance on the Faux Pas test (0.58). One of the more common explanations for this task-dependency has been differences in the complexity of theory of mind processing being assessed (Samame, 2013). False belief tasks have become the gold standard for assessing young children's understanding of mind, but these tasks only index basic mentalising, and for typically developing children, performance is significantly above chance by the age of four (Wellman et al., 2001). Although understanding false beliefs marks an important milestone in theory of mind development, it does not equip children with all they need to know about people's lives and minds. Advanced theory of mind skills develop later i.e. during middle childhood and beyond (Lagattuta et al., 2015), and are necessitated by more complex aspects of social interactions. These more advanced forms not only require participants to understand differences in belief between characters, but also require them to detect and comprehend more subtle constructs such as white lies, jokes, irony, and faux pas. An inter-related distinction also used to explain task-dependent impairments of theory of mind in bipolar disorder has been that between verbal and non-verbal tasks (Samame, 2013). For example, first-degree relatives of patients with bipolar disorder have demonstrated impaired verbal theory of mind (on the Happé Strange Stories Task), but no impairment on visual theory of mind tasks (Picture Sequencing Task, Reading the Mind in the Eyes Task)(Reynolds et al., 2014). This result was explained by the authors as reflecting the more demanding nature of the two visual tasks (cognitively and affectively demanding respectively). It is therefore a recapitulation of the distinction above, albeit in altered form.

A second distinction used to explain task-dependent theory of mind impairments is that of decoding vs. reasoning. Whereas decoding more closely approximates the perception of mental state cues, the latter places higher demands on domain-general cognitive resources such as working memory and executive function (McKinnon et al., 2013). This particular distinction provides an alternative explanation of why some studies might have failed to detect impaired affective theory of mind in euthymia, but still have evidenced impaired cognitive theory of mind (Martino et al., 2011; Barrera et al., 2013). The affective theory of mind task used in these two studies - the Reading the Mind in the Eyes Task - is essentially a measure of the ability to decode likely emotional state on the basis of perceptual information. In contrast, the cognitive theory of mind task - the Faux Pas Test - is a much more complex test requiring reasoning about whether someone said something that someone else might not want to hear. These results therefore suggest that perceptually-based theory of mind impairments may not always be detected, whilst reasoning-based theory of mind impairments may be easier to detect.

In this section, we have seen that the results of prior literature on theory of mind impairments in bipolar disorder cannot be taken at face value without considering the influence of methodological choices such as (i) the level of complexity of theory of mind being assessed, and (ii) the generic cognitive demands of the task used for assessment. In particular, some tasks are not able to detect the subtle impairments that might present in euthymic patients (Olley et al., 2005). Therefore in the future, a broader array of theory of mind tasks is warranted (Schenkel et al., 2014). In research on other populations, there have been calls for theory of mind tasks to become more ecological in nature and better mimic real-life scenarios (Garrido-Vasquez et al., 2011; Achim et al., 2013; Mathersul et al., 2013).

1.3 Cognitive and clinical correlates

In the previous section, it was suggested that the cognitive demand of different theory of mind tasks might influence the patterns of deficits observed in bipolar disorder. Indeed, a relationship between cognitive demand and theory of mind may not be surprising given the inherent overlap between neurocognition and social cognition (Van Rheenen and Rossell, 2014). So, what are the neuropsychological correlates of the theory of mind impairments? There are two important aspects to this question, first do impairments persist when neurocognitive performance is controlled for, and secondly, how does neurocognitive performance correlate with patients' capacity for theory of mind. Many correlations were reported between performance of the Reading the Mind in the Eyes task and neurocognitive function in the first such study, including correlations with sustained attention, verbal fluency and psychomotor speed (Bora et al., 2005). Further, global cognitive impairment (reduced IQ) has been shown to correlate significantly with theory of mind impairment in a recent meta-analysis (Bora et al., 2015). The co-existence of theory of mind impairments with impairments of executive functions such as inhibitory control has received further support from later research with comprehensive neurocognitive batteries (Wolf et al., 2010; Van Rheenen et al., 2014), and correlations with sustained attention impairments seem particularly strong (Lahera et al., 2008). These findings co-exist with demonstrations whereby supposed theory of mind deficits disappear once differences in neurocognition such as attention, verbal memory and visuo-spatial memory are controlled for (Martino et al., 2011; Ioannidi et al., 2015). However, this mediating role for executive functions is not a universal finding (Reynolds et al., 2014). Further, in theory of mind studies that have incorporated matched cognitive control conditions, impaired theory of mind does not necessarily co-occur with impaired performance in that control condition (Kerr et al., 2003; Van Rheenen and Rossell, 2013b). Questions therefore remain as to why this relationship is not universal. Careful more extensive research with well-powered samples is required, perhaps with neurocognitive tests that more specifically assess individual domains of executive function (Olley et al., 2005).

We next turn to consider clinical correlates of theory of mind impairments in bipolar disorder. Here the evidence is patchy, inconsistent, and incomplete, although currently available evidence does not favour reliable links with basic clinical variables (Bora et al., 2015). The only positive findings that exist so far is a possible association between performance of theory of mind tasks and illness duration (McKinnon et al., 2010; Wolf et al., 2010). Taken at face value, this suggests that theory of mind impairment is progressive, and that further study might be wise to determine in which direction the effects occur. However, elsewhere demonstration of this association has not been repeated (Martino et al., 2011), and meta-analysis of the links between socio-cognitive impairment and length of illness in bipolar disorder suggest there is insufficient evidence to take the relationship between theory of mind impairment and illness duration seriously (Samame et al., 2015). Other attempts to links basic clinical variables with theory of mind

impairment in bipolar disorder have failed to find support for an association with the number of illness episodes experienced (Bora et al., 2005;McKinnon et al., 2010;Martino et al., 2011), or age of onset (Bora et al., 2005;McKinnon et al., 2010;Wolf et al., 2010).

Perhaps more surprising has been the failure to find support for the impact of theory of mind impairment on social functioning as discussed elsewhere for other psychiatric disorders (McDonald, 2013;Pinkham, 2014;Van Rheenen and Rossell, 2014;Weightman et al., 2014). In the first study of this type, although patients with bipolar disorder in remission were impaired on a verbal theory of mind measure, the impairments showed no relationship with social and occupational functioning as indexed by the Life Functioning Questionnaire (Olley et al., 2005). Generalisability was widened with the demonstration by Barrera et al using different theory of mind and social functioning measures in which they observed that neither scores on the Reading the Mind in the Eyes Task nor scores on the Faux Pas Test correlated with global functioning according to the Functioning Assessment Short Test (Barrera et al., 2013). These two studies did, however, test euthymic patients, who are perhaps less likely to show sizeable functional impairments relative to symptomatic patients, and both assessed only a small sample of patients (N=12 and N=15 respectively). Yet similar patterns have emerged in larger datasets from symptomatic patients. In a study by Cusi et al., performance on the Reading the Mind in the Eyes Task did not correlate with any social domain on the Social Adjustment Self-Report Scale in a mixed sample of Bipolar 1 Disorder patients with varying levels of depressive symptoms (Cusi et al., 2012a). Further, a subsequent study by Benito et al. uncovered no evidence for an association between performance of the Hinting Task and global functioning according to the Functioning Assessment Short Test (Benito et al., 2013). However, a prospective study by Purcell et al. produced the interesting finding that abnormally short response times on the Reading the Mind in the Eyes Task predicted greater life functioning impairment as assessed by the Life Functioning Questionnaire (Purcell et al., 2013). Thus whilst theory of mind impairment might not predict concurrent social functioning, it may be able to predict the likelihood of further decline. Alternatively, as suggested by the authors, since the prospective relationship was with response times on the theory of mind task rather than accuracy, it may be the case that quick mental state inferences are more helpful in understanding functional impairment.

As lamented by others (Samame, 2013), only a handful of studies have investigated the potential influences of medication on theory of mind performance such as duration of exposure, dose effects, or the type of medication being taken. Yet, as can be seen from Table 1, the medication profile of participant samples is often markedly heterogeneous, both across- and within-studies, and receipt of multiple medications is common. This poses a major potential confound. Often studies are underpowered to make statistical comparisons of the effects of different classes of medication, analyses are cursory and retrospective, with possible medication effects frequently being cited as study limitations. This has, in part, resulted from the challenges associated with accessing unmedicated samples of patients with bipolar disorder and from variations in medication profile inherent to the heterogeneity of bipolar disorder. Perhaps not surprisingly, the results of ad hoc analyses have been negative where attempted. Shamay-Tsoory et al. divided their patients into three groups according to the medications being received: lithium (N=9), carbamazepine (N=6), and sodium valproate (N=4). However, these three subgroups did not differ in either cognitive or affective theory of mind performance (Shamay-Tsoory et al., 2009). Post-hoc analyses by Van Rheenen et al. also failed to detect an influence on theory of mind performance according to whether a patient was on vs. off antipsychotics, antidepressants, mood stabilisers, or benzodiazepines (Van Rheenen and Rossell, 2013b). Elsewhere, amongst people at high-risk for bipolar disorder, previous lifetime exposure to psychotropic medication (self-report) has also been shown not to influence theory of mind performance (Whitney et al., 2013). A more definitive study by Bora et al, examined correlations between serum lithium levels and theory of mind performance

on both the Reading the Mind in the Eyes Task and the Hinting Task in euthymic patients with Bipolar 1 Disorder, but did not detect any such relationship (Bora et al., 2005). Medication effects on theory of mind have also been quantified and compared using the Clinical Scale of Intensity, Frequency, and Duration of Psychopharmacological Treatment, to index current exposure to different classes of medication on a scale from 0-5. Whilst that study also failed to find evidence of medication effects in either Bipolar 1 or Bipolar 2 disorder on the Reading the Mind in the Eyes Task, a significant correlation was observed with performance on the Faux Pas test (Martino et al., 2011). Further, once exposure to benzodiazepines was controlled for, performance on the Faux Pas test no longer allowed the prediction of whether a participant was a patient or healthy control. There is currently a lack of optimism as to whether psychotropic medications such as those prescribed for bipolar disorder improve social cognition (Hempel et al., 2010; Kucharska-Pietura and Mortimer, 2013). However, as to whether these drugs worsen social cognitions such as theory of mind, further research is required.

In this section, we have seen evidence that theory of mind impairment often co-exists alongside cognitive impairments, particularly those relating to executive functions. Further, some of these cognitive impairments correlate with, or predict, the degree of theory of mind impairment. Thus there is now a sufficient evidence base to warrant further investigation to flesh out our understanding of the relationship between the two, and how the mechanism of effects fits together (Brune and Brune-Cohrs, 2006; Samame, 2013). For both therapeutic purposes and theoretical reasons, it is particularly important to establish whether theory of mind impairment in bipolar disorder is primary in origin, or simply secondary to cognitive impairment. Regarding medication effects on theory of mind, not only are they of interest in their own right, they present an important confound to the comparison of results from prior studies (Samame et al., 2012). Yet, often studies only provide broad information on the drug classes being received, without identifying the name of the specific medicine being received. This needs to be rectified, although the separate effects of specific drugs will always be difficult to tease apart where patients are concurrently in receipt of multiple medications. Regarding clinical correlates, theory of mind studies in bipolar disorder are now accumulating, but they do not always examine the relation between social cognition and clinical variables (Samame, 2013). Future research that focussed on core issues concerning the evolution of theory of mind impairment in response to changes in clinical course, could enable more responsive, dynamic and individualised patient care in social and occupational contexts (Cusi et al., 2012a).

1.4 Clinical implications and next steps

It has been recognised for some time now that establishing a clear pattern of theory of mind deficits in bipolar disorder may have profound implications for the clinical management of patients. Difficulties in understanding the mental state of others can result in the misreading of social cues, resulting in a reduced ability to accurately comprehend social interactions (Ang and Pridmore, 2009). Patients with impaired theory of mind are therefore unlikely to understand the impact of their behaviour on others, and this may contribute to their willingness to indulge in reckless or dangerous activities (Rodrigo et al., 2014; Sandvik et al., 2014). Moreover, difficulty in understanding the perspective of others may be an impediment to some psychological interventions (Fonagy and Allison, 2014; Weinstein et al., 2014). Regarding the next phase of research we make the following suggestions. First, the adoption of standardised task design would be prudent where possible, as has become commonplace for the study of child populations (Brooks and Meltzoff, 2015; Moll et al., 2015), or as afforded by well-validated tests e.g. 'The Awareness of Social Inference Test' (McDonald et al., 2003; Spunt and Adolphs, 2014), which has been extensively normed across

adolescent, young- and middle aged populations, and assessed for reliability, practice effects, and education- and IQ-independent consistency. This latter test assess the ability to perceive social inferences both with (minimal context) and without the benefit of additional information revealing the protagonist's true thoughts or feelings (enriched context), in order to assess whether participants are able to integrate and use explicit contextual information regarding speaker beliefs. Second, comprehensive neuropsychological batteries should be administered routinely alongside the theory of mind paradigms, e.g., the International Society for Bipolar Disorders-Battery for Assessment of Neurocognition (ISBD-BANC) (Yatham et al., 2010), to separate out the effects of cognitive impairment and theory of mind impairment. Third, further research should adopt more ecological theory of mind tests e.g. incorporating video-based material or virtual reality scenarios (Achim et al., 2013; Henry et al., 2015). We do not suggest that these should replace use of the controlled simplistic tasks currently in use, as these have the capacity to isolate specific individual aspects of the impairment. On the other hand, although perception of cues from isolated modalities is of theoretical interest, such an approach lacks the ecological validity of multi-modal cues in naturalistic settings. In some populations e.g. older adults, it has even been demonstrated that impairments of social cognition are reduced in magnitude when more life-like assessments are used (Hunter et al., 2010; Lambrecht et al., 2012). Related to this is the predominant use of static photographs at present. In contrast, dynamic stimuli are also ecologically valid and are information-rich, which facilitates more accurate understanding (Murphy et al., 2010; Fiorentini and Viviani, 2011; Phillips and Slessor, 2011; Ruffman, 2011). Evaluating the performance of patients with bipolar disorder when responding to theory of mind cues in more realistic situations will allow us to better understand how these impairments might translate into impairments in daily living. For example, the video modality adopted by Montag et al. for the purposes of evaluating more subtle impairments, in which participants view a film showing two women and two men spending an evening together, with the instruction to try to understand the feelings, thoughts and intentions of the characters, for the purposes of answering a series of multiple-choice questions (Montag et al., 2010). Fourth, more longitudinal studies are needed. In addition to the benefits discussed earlier, this endeavour would facilitate a better understanding of whether the deficits are static or progressive, which has important implications for characterising the natural history of bipolar disorder, its clinical management and more accurate prediction of the likely functional deficits ahead. This might be enhanced by parallel studies of changes in functional neuroanatomy over time, to help establish the underlying mechanisms of change (Cusi et al., 2012b).

2 Comparative assessments of theory of mind in bipolar disorder and schizophrenia

In terms of the type of symptoms within bipolar disorder that might associate with theory of mind impairments, there have been a number of suggestions, including impulsivity (Purcell et al., 2013; Hoertnagl and Hofer, 2014) and affect (Bora et al., 2005; McKinnon et al., 2010). However, the most prevalent discussions have centred on a possible association with psychotic symptoms or history of psychosis. Indeed it has been claimed that theory of mind impairment is characteristic of all the major psychoses, irrespective of diagnosis (Bora et al., 2009b; Guastella et al., 2013). This makes sense given the partial overlap in symptoms across schizophrenia and bipolar disorder (Lewandowski et al., 2011; Rosen et al., 2011; Wilson and Sponheim, 2014), and the common occurrence of psychosis in the manic state (Lindenmayer et al., 2008; Basso et al., 2009; Ostergaard et al., 2013). The hypothesis that theory of mind impairments might present in both schizophrenia and bipolar disorder is further motivated by the partial overlap in genetic basis between the two disorders (Tiwari et al., 2010; Cardno and Owen, 2014). Therefore we now turn to more substantive methodology, and evaluate theory of mind studies that have directly compared patients with

diagnoses of bipolar disorder against those with diagnoses of schizophrenia. We summarise reports of direct comparisons of theory of mind impairment in these two patient groups in **Table 2**. Here we do not seek to serve a review of literature on theory of mind impairments in schizophrenia per se. For that the interested reader is referred to works elsewhere (Sprong et al., 2007; Pickup, 2008; Bora et al., 2009a; Biedermann et al., 2012; Gavilan Ibanez and Garcia-Albea Ristol, 2013).

2.1 Relative scale of impairment

One of the most prominent issues amongst studies comparing performance on theory of mind tasks across bipolar disorder and schizophrenia, is the question of whether the impairments are of equal magnitude. The use of traditional theory of mind tests such as the Reading the Mind in the Eyes and the Faux Pas Tests provide some evidence that the impairments observed in schizophrenia might be greater than those in patients with bipolar disorder (Donohoe et al., 2012; Caletti et al., 2013). However, the results are not always positive. In one study, no differences in performance were observed between patients with schizophrenia vs. bipolar disorder performing the Happé Strange Stories task (Rossell and Van Rheenen, 2013). Similarly, whilst patients with schizophrenia, and bipolar patients with and without psychosis all showed deficits on the Reading the Mind in the Eyes and Hinting tasks, the level of impairment for each task was similar across the three patient groups (Thaler et al., 2013). One explanation is that if the theory of mind impairment is linked to current psychosis, the deficit should show a relationship to symptom severity irrespective of diagnosis, and therefore between-group differences might not necessarily be expected. There is certainly some supporting evidence for this (Marjoram et al., 2005; Guastella et al., 2013).

A second explanation for the variable support for theory of mind impairments being greater for schizophrenia than for bipolar disorder is that as mentioned above, these simple tests lack ecological validity (Lahera et al., 2015), which has promoted other studies wishing to compare the impairments in schizophrenia and bipolar disorder to use more ecological tests. Here, the evidence for greater impairment in schizophrenia is more convincing, which implies that patients with schizophrenia might only show greater theory of mind impairments than those in bipolar disorder on more demanding or more life-like tests (Lee et al., 2013; Rowland et al., 2013). The Versailles-Situational Intention Reading task also comprises video excerpts, and requires participants to rate the probabilities of affirmations of the intentions of different characters. With this task, a similar story emerges, and patients with schizophrenia again showed greater deficits than patients with bipolar disorder, but whilst the difference between schizophrenic and depressed patients was significant, the difference between schizophrenic and manic patients was not quite significant (Bazin et al., 2009).

2.2 Symptomatic and cognitive mediators of the differences

Given that patients with schizophrenia are sometimes more impaired than patients with bipolar disorder, the question becomes what is driving these differences? In cross-diagnosis theory of mind studies differences between the patients with schizophrenia and bipolar disorder with respect to various basic clinical factors often occur, including substance abuse (Caletti et al., 2013), and number of hospitalisations (Thaler et al., 2013). Beyond striving to match such basic clinical variables, another important target is to match for generic severe mental illness pathology, so that any differences in theory of mind impairment can then be attributed to the disorders themselves rather than generic differences in symptom severity. When theory of mind in patients with schizophrenia and bipolar disorder have been analysed taking account of broad symptom variables such as depression, positive and negative symptoms, these types of factors are not always

significant predictors of impairment (Lee et al., 2013;Thaler et al., 2014). Moreover, differences in theory of mind performance often remain significant after statistically controlling for differences in these broad measures (Donohoe et al., 2012).

Matching for level of positive symptoms at the recruitment rather than statistical analysis stage has further facilitated evaluation of theory of mind impairment according to disorder. When this approach was adopted, patients with schizophrenia still showed a greater theory of mind impairment than patients with bipolar disorder (Rossell and Van Rheenen, 2013), implying that factors other than psychosis must also contribute to differences in performance between the patient groups. Yet weight to a cross-diagnostic link between theory of mind impairment and specific positive symptoms has been provided by Marjoram et al., who evidenced such a relationship across patients with schizophrenia and a mixed group of patients with unipolar or bipolar depression. Rather than the theory of mind impairment being disease-specific and only occurring in patients with schizophrenia, they observed a cross-diagnostic symptom-specific relationship between performance of the Hinting task and positive symptoms as indexed by severity of hallucinations/delusions (Marjoram et al., 2005). A similar story emerges from other comparisons, such as the demonstration by Guastella et al. that performance of the Reading the Mind in the Eyes Test was a strong predictor of global positive symptoms across patients with likely psychotic vs. bipolar illness (Guastella et al., 2013). Interestingly, when the theory of mind performance of patients with schizophrenia who did vs. did not show evidence of thought disorder (another positive symptom) was compared to the performance of patients with bipolar disorder, it was only performance of the schizophrenic patients with thought disorder that was impaired relative to healthy controls (Sarfati and Hardy-Bayle, 1999). The performance of the patients with schizophrenia without thought disorder was comparable to that of patients with bipolar disorder, again suggesting a link between theory of mind impairment and specific symptoms of psychosis, rather than a general increase in impairment in schizophrenia.

Thus there may be two co-existing patterns of results, namely a symptom-specific relationship between theory of mind impairment and certain positive symptoms that is independent of diagnosis, and another unidentified cause of the differences. As to what the likely cause is of this other unidentified contribution to the differences, there are a number of candidates. Attributional style has been explored in patients with schizophrenia and bipolar disorder, and whilst both groups showed evidence of hostile socio-cognitive biases, theory of mind impairment on the Hinting Task was still greater in patients with schizophrenia than in bipolar disorder, thus ruling attribution style out as a possible mediator (Lahera et al., 2015). Emotion regulation has also been investigated. Whilst patients with schizophrenia showed significantly greater theory of mind impairment than those with bipolar disorder, and distinct patterns of cognitive strategies were used to regulate emotion in the two patient groups (schizophrenia: more likely to engage in catastrophising and rumination; bipolar disorder: more likely to blame themselves and less likely to engage in positive reappraisal), associations between theory of mind performance and affect regulation were not observed in either group (Rowland et al., 2013). As to the possibility that differences in medication doseage or medication type between patients with schizophrenia and bipolar disorder might influence differential theory of mind impairment, variability and multiplicity in the medications patients are receiving makes the comparison of respective medication effects difficult (Rossell and Van Rheenen, 2013;Thaler et al., 2014). However, it is perhaps unlikely that medication differences might drive differences in theory of mind performance. First, antipsychotic equivalence dosage appears to have no effect on theory of mind performance i.e. there is no evidence of correlation between the two (Sarfati and Hardy-Bayle, 1999;Marjoram et al., 2005;Donohoe et al., 2012). Second, use of antipsychotic medication did not alter the predictive power of performance on the Reading the Mind in the Eyes Test in relation to severity of positive symptoms (Guastella et al.,

2013). Thirdly, when the theory of mind performance of bipolar patients taking antipsychotics is compared to the performance of bipolar patients not taking antipsychotics, no significant differences were observed (Lee et al., 2013).

Another potential mediator of differences in theory of mind performance worthy of consideration is the differences in cognitive impairment between these two patient groups (Harvey et al., 2010; Andreou and Bozikas, 2013; Bakkour et al., 2014). This is a factor that comparative studies of theory of mind across bipolar disorder and schizophrenia do not always control for, leaving the door open for differences in cognitive function between the two groups to confound differences in theory of mind impairment. In the direct comparative literature, both differences in theory of mind impairment and in cognitive function in the verbal memory, episodic memory, working memory, attentional, visual learning, reasoning, and processing speed domains have been shown to co-exist in patients with schizophrenia vs. bipolar disorder, but the impact of specific cognitive differences on differences in theory of mind performance have not been analysed (Donohoe et al., 2012; Caletti et al., 2013; Lee et al., 2013). The evidence for a differential influence of general cognitive ability initially appears a little stronger, since IQ has been shown to correlate with performance of the Reading the Mind in the Eyes Test in patients with schizophrenia but not in patients with bipolar disorder, and vice versa for performance of the Hinting Task (Donohoe et al., 2012). However, the inclusion of IQ when analysing differences in theory of mind does not tend to change the pattern of differences observed for the two disorders (Donohoe et al., 2012; Rossell and Van Rheenen, 2013).

2.3 The implications of differential impairments

In the literature focussing exclusively on bipolar disorder, moves to link the experience of psychosis with increased theory of mind impairment have, although derived from a strong rationale, have not yet been particularly productive. Bora et al. found no impact of history of psychosis on performance of the Hinting Task when comparing twenty six patients with such a history to 17 patients with no past history, but at the time of testing the patients were euthymic (Bora et al., 2005). However, in another study, performance of that task by symptomatic patients showed no difference between patients with and without past history of psychosis (Benito et al., 2013). The same pattern has been noted for other theory of mind tests such as the Happé Strange Stories Task (Lahera et al., 2008), and for the relationship of history of psychosis to cognitive and affective theory of mind (Barrera et al., 2013), and for both Bipolar 1 and Bipolar 2 Disorder (Martino et al., 2011). It might therefore be concluded that theory of mind deficits do not constitute a vulnerability marker for psychosis. However, in schizophrenia itself, theory of mind deficits lessen when patients are in remission (Bora et al., 2009a; Wang et al., 2013). Thus seeking to link deficits to a history of psychosis once bipolar patients are no longer experiencing psychosis may be less likely to succeed than if testing patients currently experiencing psychosis. We might not yet be using the most optimal methods to evaluate the research questions being pursued in this field.

In the first part of this review, we considered whether theory of mind impairment could be a trait marker for bipolar disorder across different mood states. Here the question is could a theory of mind impairment go one step further, and serve as a useful cognitive endophenotype of proneness to psychosis? There are certainly examples of *non-social* cognition being accepted as candidate endophenotypes for bipolar disorder and schizophrenia (Raust et al., 2014; Reilly and Sweeney, 2014), and if theory of mind impairments prove to be an endophenotype for the psychoses, this knowledge could ultimately aid in efforts to identify risk-related genes for this group of disorders, as well as in prevention and early intervention. At present, yes theory of mind impairments are

present in both schizophrenia and bipolar disorder, but attempts to link these findings as originating from a common (genetic) cause have not yet been as successful as was hoped (Lee et al., 2013). It remains to be proven unequivocally that theory of mind impairment in bipolar disorder and schizophrenia occurs specifically because the two are both types of psychosis (Lee et al., 2013). Future studies might benefit from expanding the comparisons to explore theory of mind impairment in other related disorders such as schizoaffective disorder, schizophreniform disorder, and schizotypal personality disorder (Bora et al., 2009b; Bora and Pantelis, 2013).

Despite the uncertain nature of the association of theory of mind impairment across the two affective and non-affective psychoses, given the potential for socio-cognitive deficits to impact on social and occupational function, their comparison remains important, because it may partly explain differences in outcome between the disorders (Donohoe et al., 2012). For this same reason, reliably identified differences among diagnoses may be crucial to pinpoint treatment planning, medication management, and long-term patient care (Thaler et al., 2013). Establishing differences in social functioning might also be indicative of the likely success of remediation through recent socio-cognitive training schemes that aim to improve abilities such as theory of mind (Brown et al., 2012; Fiszdon and Reddy, 2012; Kurtz and Richardson, 2012; Lahera et al., 2013). It has been claimed that socio-cognitive impairments such as theory of mind may be less of a determinant of functioning in bipolar disorder than in schizophrenia, and therefore that *non-social* cognitive remediation may be better suited for bipolar disorder (Lee et al., 2013). However, there has been little direct comparison of the links between theory of mind impairment and social functioning in the two patient groups. In the study by Caletti et al., patients with bipolar disorder showed greater social functioning according to the DSM General Assessment of Functioning Scale (American Psychiatric Association, 2013), level of functioning was then shown to correlate with theory of mind score, and impairments on the Reading the Mind in the Eyes Test and Faux Pas Test were worse in schizophrenia than in bipolar disorder (Caletti et al., 2013). It can be inferred from these data that the impact of theory of mind impairment on functioning that patients with schizophrenia experience might be greater than that experienced in bipolar disorder, simply because they have a greater theory of mind deficit. Although the correlations were not examined separately in each patient group, this was performed in a separate study in which better theory of mind performance predicted better functioning, but only for the patients with schizophrenia, not for those with bipolar disorder (Thaler et al., 2014). So, the early signs are that theory of mind impairment does indeed have more of an impact on everyday functioning in schizophrenia than in bipolar disorder.

3 Conclusions

This theoretical review has attempted to synthesise the existing data examining the ability of people with bipolar disorder to deduce the feelings and intentions of other minds via 'theory of mind', and what has been learned from the comparative study vs. the abilities of people with schizophrenia. In drawing the literature together, a number of themes were identified. In part one these included the generalisability of impairments across different presentations of bipolar disorder, changes in impairment according to the type of theory of mind and the task used for assessment, the influence of cognitive impairment and relationship to illness variables, and the prominent suggestion of a relationship to history of psychotic symptoms. Then in part two, the prominent themes included a smaller theory of mind impairment in patients with bipolar disorder vs. schizophrenia, the relationship to differences in symptoms and cognitive impairments between the disorders, and the likely consequences of the differences in theory of mind impairment for the clinical management of patients with bipolar disorders vs. schizophrenia.

Due to many of the complexities discussed during this theoretical review, our understanding of theory of mind impairment in bipolar disorder is not yet complete or consolidated, and further research will be required before our knowledge reaches the advanced state of the literature relating to schizophrenia. However, currently available data suggest the following trends. First, although consistent differences in impairment between the mood states remain elusive, there is convincing evidence that theory of mind is impaired in some way across the mood states, and into the supposedly asymptomatic state of euthymia. It may therefore be considered a trait rather than state impairment, i.e. one that is an enduring correlate of bipolar disorder. Given that the structural neuroanatomical abnormalities associated with bipolar disorder include regions crucial for the mediation of theory of mind e.g. medial prefrontal cortex (Savitz et al., 2014), this is perhaps not surprising. Genome-Wide Association Studies have similarly identified an enduring genetic association between the ZNF804A risk-variant known to increase susceptibility for bipolar disorder and the phenotype for (ab)normal functional connectivity during theory of mind (Gurung and Prata, 2015). As to methodological generalisation, given that the processing of emotion cues and some of the common neurocognitive sub-processes e.g. 'representing mental states with propositional content' needed for any form of meta-representation (Schurz and Perner, 2015) are compromised in patients with bipolar disorder (Townsend and Altshuler, 2012; Van Rheen and Rossell, 2013a; Atagun et al., 2014; Fung et al., 2015), it is likely that further research with sensitive methodology will likely demonstrate impairment across both cognitive and affective theory of mind. We further predict that the possible inter-dependence of impairments in executive functions and theory of mind will eventually prove fruitful given the strong evidence elsewhere for a deterministic relationship between the two processes throughout normal development (Devine and Hughes, 2014; Moriguchi, 2014).

Although this review was wide-ranging, it has highlighted a number of pertinent gaps in the field, and has identified a number of possible future directions. A more comprehensive understanding of theory of mind impairments in bipolar disorder will be of great clinical utility in devising improved psychological or cognitive therapies that assist patients with everyday life skills. Whilst early studies of bipolar disorder have not yet established a clear relationship between these impairments and functional outcome, it is known from other patient populations that impaired theory of mind is a crucial factor underlying poor life skills, poor social cognition and some aspects of psychosis. Based on this wider evidence set, a phenomenon with this potential impact is deserved of further study. Ultimately, if a lack of relationship between theory of mind impairment and functional outcome were perpetuated by increasingly sophisticated methods, the question of interest then becomes what other factor is protecting patients with bipolar disorder against the potential for theory of mind impairment to compromise functional outcome. As to the question of what should be done about theory of mind impairments in bipolar disorder, by understanding the cognitive mechanisms that underlie theory of mind impairment, reformulations as to how to remediate these skills are facilitated. There is certainly optimism about possible remediation in the literature on theory of mind in bipolar disorder (Cusi et al., 2012b; Schenkel et al., 2014), just as there has been for the improvement of theory of mind in schizophrenia. Here, close examination of developments in the literature on social cognition remediation in schizophrenia will likely be of great inspiration. Indeed there has already been one successful report of the benefits of a remediation programme originally developed for use with patients with schizophrenia being transferable to patients with a diagnosis of bipolar disorder (Lahera et al., 2013). If the neurodevelopmental nature of schizophrenia and its timing mitigate against acquisition of theory of mind to some degree (Korkmaz, 2011), the less pronounced neurodevelopmental processes behind adult forms of bipolar disorder could be taken to indicate an even greater potential for therapeutic success in attempts to remediate theory of mind impairment in bipolar disorder. Given our increased understanding of the neurobiological networks involved in theory of mind, neuroimaging research will help elucidate the

737 dysfunctional underlying brain mechanisms across the psychoses, and thereby further contribute to
738 new advances in the treatment of bipolar disorder.

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Provisional

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Provisional

Study	Sample ¹	Diagnostic Criteria	Participant Characteristics	Medication Details	Task ²	Key Results
<i>Barrera et al. (2013)</i>	N=12 EUTH (7 BP1, 5 BP2); N=12 HC	DSM-IV and ICD-10; outpatients.	EUTH: mean age 48.2 yrs; 100% M/0% F. HC: mean age 46.0 yrs; 100% M/0% F.	Mood stabilisers (10/12), atypical antipsychotics (5/12), sedatives (4/12).	The Reading the Mind in the Eyes Test; the Faux Pas Recognition Test.	Trend towards impaired cognitive ToM, and trend towards association with higher number depressive episodes. Affective ToM not impaired. No correlation between functionality and ToM.
<i>Benito et al (2013)</i>	N=44 BD (39 BP1, 6 BP2); N=48 HC	DSM-IV-TR; stable outpatients.	BP: mean age 42.3 yrs; 36.4% M/ 63.6% F. HC: mean age 45.7 yrs; 37.5% M/ 62.5% F.	Not specified.	The Hinting Task.	Patients' verbal ToM impaired relative to HC. Performance not correlated with global functioning.
<i>Bora et al. (2005)</i>	N=43 EUTH (BP1); N=30 HC	DSM-IV; in- vs. out-patients not specified.	EUTH: mean age 38.6 yrs; 53% M/ 47% F. HC: mean age 38.9 yrs; 43% M/ 57% F.	All patients treated with mood stabilisers. Atypical antipsychotic (6/43); antidepressant (2/43); mood stabiliser only (28/43); mood stabiliser and anticonvulsant (9/43); mood stabiliser and antipsychotic (6/43).	The Reading the Mind in the Eyes Task; the Hinting Task.	EUTH impaired on both ToM tasks. No effects gender or drug treatment, clinical variables, nor history psychosis. Some correlations with executive function.
<i>Cusi et al. (2012)</i>	N=25 BP (17 BP1, 7 BP2, 1 BPnos; 10 EUTH, 12 DEPsub, 3	DSM-IV; mixed inpatients and outpatients.	BP: mean age 45.2 yrs; 28% M/72% F. HC: mean age 44.2 yrs; 28%	Mood stabiliser (11/25); anticonvulsant (22/25); antidepressants (14/25); typical antipsychotics (3/25); atypical	The Reading the Mind in the Eyes Task.	BP impaired. Performance associated with illness duration. Performance not associated with social functioning.

	DEPmod); 25 HC		M/72% F.	antipsychotics (18/25); sedatives (22/25); no medication (1/25).		
<i>Inoue et al. (2004)</i>	N=50 AFF euth (34 MDD; 16 BP); N=50 HC	DSM-IV; in- vs. out-patients not specified.	EUTH: mean age 44.5 yrs; 56% M/44% F. HC: mean age 38.9 yrs; 56% M/44% F.	All patients receiving medication. Antidepressants (49/50); typical antipsychotic (6/50); atypical antipsychotic (4/50).	Custom-made picture sequencing task using caricatures and verbal descriptions, followed by first- and second-order ToM questions.	AFF impaired on second-order ToM only. No correlations with IQ.
<i>Ioannidi et al. (2015)</i>	N=29 BP1 (in both a symptomatic and euthymic phase); N=29 HC	DSM-IV-TR; in- vs. out-patients not specified.	BP1: mean age 44.2 yrs; 41.4% M/58.6% F. HC: mean age 44.9 yrs; 41.4% M/58.6% F.	All patients receiving mood stabilisers. Majority also received antipsychotics, antidepressants or benzodiazepines.	Two stories examined ability to appreciate first-order false beliefs; the Hinting Task; the Faux Pas recognition task.	Significantly lower performance in all ToM tests during acute phases vs. HC. Only impaired on Faux Pas test in euthymic phase. Faux Pas test impairments not significant when neuropsychological performance accounted for.
<i>Kerr et al. (2003)</i>	N=20 MAN; N=15 DEP; N=13 EUTH; N=15 HC	DSM-IV; mixed inpatients and outpatients.	MAN: mean age 41.3 yrs; 55% M/45% F. DEP: mean age 45.1 yrs; 52.5% M/47.5% F. EUTH: mean age 46.8 yrs; 46.7% M/53.3% F. HC: mean age 36.0 yrs; 46.7%	Mood stabiliser (47/48-collapsed across groups). MAN: antipsychotics (20/20); antidepressants (1/20); anticonvulsants (5/20). DEP: antipsychotics (7/15), antidepressants (4/15); anticonvulsants (3/15).	Six stories examined ability to appreciate first- and second-order false beliefs and deceptions. Stories read aloud with concurrent presentation cartoon drawings depicting action sequences.	Impaired 1 st and 2 nd order ToM performance for DEP and MAN even when memory controlled for. MAN performance worse than DEP. EUTH not impaired.

			M/53.3% F.	EUTH: antipsychotics (4/13), antidepressants (1/13); anticonvulsants (1/13).		
<i>Laheara et al. (2008)</i>	N=42 EUTH with psychosis; N=33 EUTH without Psychosis; N=48 HC.	DSM-IV-TR; stable outpatients.	EUTH with psychosis: mean age 45.8 yrs; 33.3% M/66.7% F. EUTH without psychosis: mean age 51.2 yrs; 48.5% M/51.5% F. HC: mean age 46.6 yrs; 33.3% M/ 66.7% F.	No between-group differences in mean number drugs received. Regarding type, EUTH with psychosis received mood stabiliser and antipsychotic combination with higher frequency than EUTH without. Patients without psychosis on mood stabilisers with higher frequency than EUTH with psychosis.	The Strange Stories Task.	Performance similar in bipolar patients with or without psychosis. Both impaired relative to HC. Impairments partly explained by general cognitive deficit.
<i>Martino et al. (2011)</i>	N=45 BP1; N=36 BP2; N=34 HC.	DSM-IV; outpatients.	BP1: mean age 37.2 yrs; 44.5% M/55.5% F. BP2: mean age 42.9 yrs; 22.3% M; 77.7% F. HC: mean age 39.7 yrs; 35.3% M/64.7% F.	All patients receiving mood stabilisers. Additionally 36% were receiving antidepressants, 48% benzodiazepines, and 54% antipsychotics. BP had higher exposure to antipsychotics than BP2. No differences between BP1 and BP2 in exposure to other psychotropic	The Faux Pas test; the Reading the Mind in the Eyes Task.	Both BP1 and BP2 impaired relative to HC. When neurocognitive impairments and exposure to medications controlled, performance did not predict whether patient or HC. Impaired ToM partly mediated by executive function deficits and exposure to psychotropic medications.

				medications. BP1 had higher dose antipsychotics BP2.		
<i>McKinnon et al. (2010)</i>	N=14 BPSUB (8 BP1, 5 BP2, 1 BPnos); N=14 HC	DSM-IV; in- vs. out-patients not specified.	BPSUB: mean age 47.5 yrs; 28.6% M/71.4% F. HC: mean age 43.1 yrs; 35.7% M/64.3% F.	All patients receiving medication. Mood stabiliser (7/14); anticonvulsants (6/14); antipsychotics (8/14); antidepressants (7/14); sedatives (10/14); stimulant (1/14).	Custom-made test with scenarios describing complex social situations such as faux pas, followed by first- and second-order ToM questions.	Patients impaired on cognitively demanding second-order ToM . Reduced performance associated with longer illness duration, and increased symptom severity.
<i>Montag et al (2010)</i>	N=29 EUTH; N=29 HC	DSM-IV; outpatients.	EUTH: mean age 44.0 yrs; 34.5% M/65.5% F. HC: mean age 39.7 yrs; 44.8% M/55.2% F.	All patients receiving medication. Mood stabiliser (9/29); anticonvulsant (17/29); atypical antipsychotic (13/29); antidepressant (11/29); sedatives (2/29).	The Movie for the Assessment of Social Cognition	EUTH performed worse than HC for cognitive ToM, but not for affective ToM. EUTH showed higher 'undermentalising' but not higher 'overmentalising'. Number manic episodes correlated with 'undermentalising' and affective ToM.
<i>Olley et al. (2005)</i>	N=15 EUTH (BP1); N=13 HC	DSM-IV; outpatients.	EUTH: mean age 39.2 yrs; 46.7% M/53.3% F. HC: mean age 40.8 yrs; 46.1% M/53.9% F.	Stable medication regime for 6 weeks. Number of Years' exposure to psychotropic medications recorded but not reported. Medication effects not examined due to different combinations	The Strange Stories Task. Also a custom-made cartoon comprehension task that required ToM to interpret correctly.	Impaired relative to HC on verbal ToM. Although performance comparable to HC for non-verbal ToM, responses slower. ToM did not correlate with social or occupational functioning, but some correlations with executive function.

				mood stabilisers, antidepressants, and antipsychotics.		
<i>Purcell et al. (2013)</i>	N=29 EUTH; N=28 HC	DSM-IV-TR; outpatients.	EUTH: mean age 29.6 yrs; 35% M/65% F. HC: mean age 32.1 yrs; 36% M/63% F.	Mean number of psychotropic medications currently taken, including anticonvulsants, mood stabilisers, antipsychotics, stimulants, antidepressants, and sedatives = 2.04.	The Reading the Mind in the Eyes Task.	EUTH responded faster in comparison to HC. Performance accuracy no different though. Faster response times predicted increased overall life functioning impairment.
<i>Reynolds et al. (2014)</i>	N=20 BD; N=20 HC	NB, first-degree relatives of patients with specified DSM-IV-TR diagnosis.	NB, children of mothers with specified DSM-IV diagnosis.	NA	The Strange Stories Task; the Picture Sequencing Task; the Reading the Mind in the Eyes Task.	BP impaired on verbal ToM, but not visual or higher-order ToM tasks.
<i>Schenkel et al. (2008)</i>	N=26 BD; N=20 HC	DSM-IV; outpatients.	BP: mean age 13.2 yrs; 62% M/38% F. HC: mean age 13.0 yrs; 55% M/45% F.	Medication-free at least 1 week prior to testing.	Custom-made measure false-belief understanding ('Affective Story Task'). Stories of emotionally-charged situations read aloud, participants asked false-belief question to assess whether understood potential for misunderstanding. The Hinting Task.	BP impaired relative to HC in positive and negative conditions of Affective Story Task. BP also worse than HC on Hinting Task. Performance associated with younger age, earlier illness onset and manic symptoms.
<i>Schenkel et al.</i>	N=17 BP1; N=8 BP2;	DSM-IV; outpatients.	BP1: mean age 11.4 yrs; 58.8%	Majority patients medicated but receiving	The Reading the Mind in the Eyes Task; the	BD1 worse than HC on Reading Mind in the Eyes

(2014)	N=25 HC		M/41.2% F. BP2: mean age 13.4 yrs; 100% M/0% F. HC: mean age 12.4 yrs; 64% M/36% F.	different classes medications (atypical antipsychotics, mood stabilisers, or both).	Cognitive and Emotional Perspective Taking Task.	Task, and cognitive (but not emotional) condition of Cognitive and Emotional Perspective-Taking Task.
<i>Shamay-Tsoory et al. (2009)</i>	N=19 EUTH (BP1); N=20 HC.	DSM-IV; in- vs. out-patients.	EUTH: mean age 40.2 yrs; 52.6% M/47.4% F. HC: mean age 32.6 yrs; 55% M/45% F.	All patients receiving medication (mainly mood stabilisers), medication intake stable during preceding month.	The Social Stories Test.	Impaired cognitive ToM, but not affective ToM. Performance not related to performance of neurocognitive tests. Mood stabilising sub-groups had no effect on ToM.
<i>Terrien et al. (2014)</i>	N=316 HC	Hypomanic Personality Scale; Beck Depression Inventory.	HC: mean age 23.3 yrs; 20.9% M/79.1% F.	NA	The Yoni task.	Males: Mood vitality and excitement sub-scale predicted performance. Females: No sub-scales predicted performance.
<i>Van Rheenen & Rossell (2013)</i>	N=49 BP (16 DEP, 4 MAN, 12 MIX, 17 EUTH; 37 BD1, 12 BD2); N=48 HC	DSM-IV-TR; outpatients.	BP: mean age 38.5 yrs; 48.5% M/51.5% F. HC: mean age 34.7 yrs; 58.1% M/41.9% F.	Antipsychotics (31/49); antidepressants (15/49); mood stabilisers (16/49); sedatives (10/49).	The Picture Sequencing Task.	BP performed worse than HC for ToM-relevant false-belief stories, but not on control stories. No differences in performance of symptomatic vs. euthymic patients, or BD1 vs. BD2.
<i>Van Rheenen et al. (2014)</i>	N=51 BP; N=52 HC	DSM-IV-TR; outpatients.	BP: mean age 38.5 yrs; 33.3% M/66.7% F. HC: mean age	Antipsychotics (33/51); antidepressants (16/51); mood stabilisers (16/51); sedatives	The Picture Sequencing Task.	Neurocognition associated with ToM, but social cognition not associated with emotion regulation.

			34.0 yrs; 38.5% M/61.5% F.	(10/51).		
<i>Whitney et al. (2013)</i>	N=24 BP; N=27 HC	NB, children of mothers with specified DSM-IV diagnosis. Evidence of mood dysregulation, but not fully syndromal BP.	BP: mean age 12.7 yrs; 54% M/46% F. HC: mean age 13.3 yrs; 40% M/60% F.	68% lifetime exposure to psychotropic medications.	ToM subtest of NEPSY II (developmental NEUROPSYchological assessment).	No differences between BP and HC.
<i>Wolf et al. (2010)</i>	N=33 BP (12 DEP, 10 MAN, 11 EUTH); N=29 HC.	DSM-IV; in- vs. out-patients not specified.	BP: mean age 47.7 yrs; 33.3% M/66.7% F. HC: mean age 37.0 yrs; 34.5% M/65.5% F.	Mood stabilisers (18/33), atypical antipsychotics (28/33), antidepressants (15/33).	Comic-strip task based in part on the Picture Sequencing Task, in which participants sequence cartoon stories and asked questions about characters' mental states.	BP and all clinical sub-groups impaired on all measures, but did not differ from each other in most ToM scores. Poorer performance on executive tasks did not fully explain impairments.

Table 1. Overview of theory of mind research in studies assessing patients with bipolar disorder without direct comparison to patients with schizophrenia.

AFF = affective disorder; BP = bipolar disorder; BP1 = bipolar I disorder; BP2 = bipolar II disorder; BPnos = bipolar disorder not otherwise specified, BPSub = sub-syndromal bipolar disorder; DEP = depressed bipolar patients, DEPSub = sub-syndromal depression; DEPmod = moderate depression; EUTH = euthymic bipolar patients; HC = healthy adult controls, MDD = major depressive disorder; MAN = manic bipolar patients; MIX = bipolar patients showing signs of both mania and depression.

¹ Patient groups outside of the bipolar disorders not included.

² Non-theory of mind tasks not included.

Study	Sample ¹	Diagnostic Criteria	Participant Characteristics	Details of Medication Supplied	ToM Task ²	Key Results
<i>Bazin et al. (2009)</i>	N=15 MAN; N=12 DEP; N=15 SCHIZ; N=12 HC.	DSM-IV; stable outpatients.	MAN: mean age 36.1 yrs; 86.7% M/13.3% F. DEP: mean age 46.7 yrs; 50% M/50% F. SCHIZ: mean age 35.4 yrs; 12M/3F. HC: mean age 30.1 yrs; 5M/10F.	MAN/DEP: mood stabilisers, antipsychotics and/or antidepressants. SCHIZ: antipsychotics.	The Versailles-Situational Intention Reading task (V-SIR): Video excerpts depicting complex real-life scenes social interactions. Also non-verbal comic-strip task (see Sarfati entry below).	MAN impaired relative to HC. Performance of MAN and DEP not distinguishable. Trend towards SCHIZ performing worse than MAN. No effect of group for comic-strip task.
<i>Caletti et al. (2013)</i>	N=18 EUTH (10 BP1, 8 BP2); N=30 SCHIZ; N=18 HC.	DSM-IV-TR; outpatients.	EUTH: mean age 42.2 yrs; 22.2% M/77.8% F. SCHIZ: mean age 42.5; 80% M/20% F. HC: mean age 36.1; 33.3% M/66.7% F.	EUTH: atypical antipsychotic (16/18); typical antipsychotic (3/18); mood stabiliser (18/18); antidepressant (8/18); sedative (5/18). SCHIZ: atypical antipsychotic (19/30); typical antipsychotic (11/30); Mood stabiliser (4/30); antidepressant (2/30); sedative (8/30).	The Reading the Mind in the Eyes Task; the Faux Pas test.	Both SCHIZ and EUTH performed worse than HC. SCHIZ performed worse than EUTH in both tasks.
<i>Donohoe et al. (2012)</i>	N=132 BP; N=208 SCHIZ; N=132 HC.	DSM-IV; outpatients.	BP: mean age 44.8 yrs; 54.5% M/45.5% F. SCHIZ: mean age 41.1 yrs; 72.3% M/27.7% F. HC: mean age 37.5	BP: 269.8 mg chlorpromazine equivalents. SCHIZ: 555.9mg chlorpromazine equivalents.	The Reading the Mind in the Eyes Task; the Hinting Task.	BP impaired on Reading the Mind in the Eyes Task; performance comparable to SCHIZ. More subtle impairment in BP relative to SCHIZ for Hinting Task.

			yrs; 39.9% M/60.1% F.			
<i>Doody et al. (1998)</i>	N=12 AFF (10 MDD/2 DEP); N=28 SCHIZ. No HC.	DSM-III-R. BP: inpatients; SCHIZ outpatients.	AFF: mean age 42.3 yrs, 8.3% M/91.7% F. SCHIZ: mean age 46.3 yrs; 60.7% M/39.3% F. HC: mean age 20.4 yrs; 45% M/55% F.	Not specified.	The Sally-Anne Task (first-order ToM); the Ice-Cream Van Test (second-order ToM).	Both SCHIZ and AFF performed Sally-Anne Task normally. SCHIZ impaired on Ice-Cream Van Test, but not AFF.
<i>Guastella et al. (2013)</i>	N=40 BP; N=23 SCHIZ/FEP/SAD. No HC.	DSM-IV-TR; stable outpatients.	BP: mean age 21.7 yrs; 27% M/73% F. SCHIZ/FEP/SAD: mean age 22.8 yrs; 83% M/17% F.	BP: antipsychotic (24/40); antidepressant (24/40); mood stabiliser (16/40). SCHIZ/FEP/SAD: antipsychotic (20/23); antidepressant (3/23); mood stabiliser (1/23).	The Reading the Mind in the Eyes Task.	SCHIZ/FEP/SAD more impaired than BP. Across diagnostic groups, performance correlated with psychotic but not affective symptoms.
<i>Lahera et al. (2015)</i>	N=46 BP; N=49 SCHIZ; N=50 HC.	DSM-IV-TR; stable outpatients.	BP: mean age 38.6 yrs; 37% M/63% F. SCHIZ: mean age 40.4 yrs; 57.1% M/42.9% F. HC: mean age 43.3 yrs; 42% M/58% F.	BP and SCHIZ: receiving unspecified pharmacological treatment.	The Hinting Task.	SCHIZ performed worse than BP and HC. BP also worse than HC.
<i>Lee et al. (2013)</i>	N=68 BP (52 EUTH); N=38 SCHIZ; N=HC.	DSM-IV; stable outpatients.	BP: mean age 43.9 yrs; 54.4% M/45.6% F. SCHIZ: mean age 44.7 yrs; 55.3% M/44.7% F. HC: mean age 41.4 yrs; 55.6% M/44.4% F.	BP: Antipsychotic (41/68); Lithium (13/68). SCHIZ: Antipsychotic (38/38).	The Awareness of Social Inference Test.	On lie and sarcasm subscales, BP not impaired relative to HC, but SCHIZ performed better than BP and SCHIZ.
<i>Marjoram</i>	N=15 AFF (7 BP, 8	DSM-IV;	AFF: mean age 41.7	AFF: Antidepressant only	The Hinting	BP not impaired relative

<i>et al.</i> (2005)	MDD); N=15 SCHIZ; N=15 HC.	mixed inpatients and outpatients.	ys; 40% M/60% F. SCHIZ: mean age 28.3 yrs; 86.7% M/13.3% F. HC: mean age 34.3 yrs; 66.7% M/33.3% F.	(9/15); Antidepressant and typical antipsychotic (5/15); antidepressant and atypical antipsychotic (1/15). SCHIZ: Typical antipsychotic only (4/15); typical antipsychotic and anticholinergic (5/15); atypical antipsychotic only (5/15); atypical antipsychotic and anticholinergic.	Task.	to HC. SCHIZ worse than HC and AFF. Across diagnostic groups, performance correlated with psychotic (delusions and hallucinations) but not negative symptoms.
<i>Maróthi & Kéri</i> (2014)	N=23 BP; N=28 SCHIZ; N=29 HC.	NB, children of mothers with specified DSM-IV diagnosis.	BP: mean age 10.8 yrs; 78.3% M/21.7% F. SCHIZ: mean age 10.6 yrs; 71.4% M/28.5% F. HC: mean age 10.6 yrs; 55.2% M/44.8% F.	N/A	The Reading the Mind in the Eyes Task.	SCHIZ impaired, but BP no different to HC.
<i>Pawlby et al.</i> (2010)	N=23 DEP; N=12 MAN; N=15 SCHIZ; N=49 HC.	DSM-IV; inpatients on mother and baby unit.	DEP: mean age 32.2 yrs; 100% F. MAN: mean age 29.0 yrs; 100% F. SCHIZ: mean age 30.5 yrs; 100% F. HC: mean age 30.5 yrs; 100% F.	Not specified, but mothers undergoing current treatment for a psychiatric condition excluded.	5-min video recordings of unstructured play session with baby coded.	Relative to HD, DEP less likely to comment on baby's mental state. SCHIZ interactional behaviour no different to HC.
<i>Rossell & Van Rheenen</i> (2013)	N=28 MAN; N=30 SCHIZ; N=29 HC.	DSM-IV; mixed inpatients and outpatients.	MAN: mean age 38.3 yrs; 40% M/60% F. SCHIZ: mean age 36.5 yrs; 63.3%	MAN: mood stabiliser (5/28); atypical antipsychotic (5/28); typical antipsychotic (1/28); mood stabiliser and atypical antipsychotic (8/28); mood	The Strange Stories Task.	Both patient groups equally impaired. Reduced ToM performance correlated with delusion severity in

			M/36.7% F. HC: mean age 35.9 yrs; 65.5% M/34.5% F.	stabiliser and antidepressant (4/28); typical antipsychotic and atypical antipsychotic and anticonvulsant (1/28); atypical antipsychotic and antidepressant (1/28); anticonvulsant and antidepressant (1/28); no medication (3/28). SCHIZ: atypical antipsychotics (21/30); typical antipsychotics (7/30); no medication (2/30).		MAN only.
<i>Rowland et al. (2013)</i>	N=33 BP1; N=56 SCHIZ; N=58 HC.	DSM-IV; outpatients.	BP1: mean age 40.7 yrs; 54.3% M/45.7% F. SCHIZ: mean age 44.6 yrs; 57.1% M/42.9% F. HC: mean age 33.9%; 50% M/50% F.	BP1: antipsychotic (2/33); mood stabiliser (7/33); antipsychotic and mood stabiliser (10/33); antidepressant and mood stabiliser (7/33); antipsychotic and antidepressant and mood stabiliser (2/33). SCHIZ: antipsychotic (18/56); antipsychotic and antidepressant (18/56); antipsychotic and mood stabiliser (5/56); antipsychotic and antidepressant and mood stabiliser (7/56).	The Awareness of Social Inference Test.	Both BP1 and SCHIZ impaired, SCHIZ worse than BP1.
<i>Sarfati & Hardy-Baylé (1999)</i>	N=10 MAN; N=15 SCHIZ with disorganisation; N=10 SCHIZ without disorganisation; N=15 HC.	DSM-IV; inpatients.	MAN: mean age 33.9 yrs; 60% M/40% F. SCHIZdis: mean age 35.7 yrs; 33.3% M/66.7% F. SCHIZnodis: mean age 29.2 yrs; 20% M/80% F.	MAN: antipsychotic (9/10). SCHIZ: antipsychotic (24/25). No difference in dose between groups.	Custom-made comic strip task; participants select card (from four) most likely to be last cartoon drawing.	No impairments in MAN. SCHIZ with disorganisation performed worst.

			HC: mean age 28.6 yrs; 33.3% M/66.7% F.			
<i>Thaler et al. (2013)</i>	N=24 BP1 with psychosis; N=24 BP1 without psychosis; N=30 SCHIZ; N=24 HC.	DSM-IV; stable patients, but inpatients vs. outpatients not specified.	BP1 with psychosis: mean age 37.6 yrs; 25% M/75% F. BP1 without psychosis: mean age 34.1 yrs; 42% M/58% F. SCHIZ: mean age 47.9 yrs; 66% M/33% F. HC: mean age 36.1 yrs; 46% M/54% F.	BP1 with psychosis: antipsychotic (14/24); anticonvulsant (13/24); antidepressant (10/24); mood stabiliser (5/24). BP1 without psychosis: antipsychotic (8/24); anticonvulsant (8/24); antidepressant (10/24); mood stabiliser (2/24). SCHIZ: antipsychotic (29/30); anticonvulsant (19/30); antidepressant (13/30); mood stabiliser (2/30).	The Reading the Mind in the Eyes Task; the Hinting Task.	All clinical groups performed worse than HC, but at similar level to one another.
<i>Thaler et al. (2014)</i>	N=24 BP with psychosis; N=24 BP without psychosis; N=30 SCHIZ. No HC.	DSM-IV; stable patients, but inpatients vs. outpatients not specified.	BP1 with psychosis: mean age 37.6 yrs; 25% M/75% F. BP1 without psychosis: mean age 34.1 yrs; 42% M/58% F. SCHIZ: mean age 47.9 yrs; 66% M/33% F.	BP with psychosis: antipsychotic (8/24); anticonvulsant (8/24); antidepressant (10/24); mood stabiliser (2/24). BP without psychosis: antipsychotic (14/24); anticonvulsant (13/24); antidepressant (10/24); mood stabiliser (5/24). SCHIZ: antipsychotic (29/30); anticonvulsant (19/30); antidepressant (13/30); mood stabiliser (2/30).	The Reading the Mind in the Eyes Task; the Hinting Task.	ToM only predicted functional capacity for SCHIZ.

Table 2. Overview of theory of mind research in studies assessing patients with bipolar disorder with direct comparison to patients with schizophrenia*.

AFF = affective disorder; BP = bipolar disorder; BP1 = bipolar I disorder; BP2 = bipolar II disorder; DEP = depressed bipolar patients, DYS = Dysthymia; EUTH = euthymic bipolar patients; FEP = First-episode Psychosis; HC = healthy adult controls, MAN = manic bipolar patients, SAD = Schizoaffective Disorder; SCHIZ = patients with schizophrenia.

¹ *Patient groups outside of the bipolar disorders and the psychoses not included.*

² *Non-theory of mind tasks not included.*